

Pre-Surgery Allergic and Immunologic Risk Assessment

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AAAAI

**3611. AHP: Pre-Surgery Allergic and
Immunologic Risk Assessment**

*Sunday, March 20, 2011, 2:00 pm - 3:15 pm
Hilton, Continental 1, Ballroom Level*

Perioperative Anaphylaxis

Specific allergic risk assessment and management

- Symptom presentation
- Agents
- Populations at risk 

Common variable immunodeficiency

Mastocytosis

Mast cell activation syndrome

Risk Assessment for Allergic Complications During the Perioperative Period

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Outline

- **General Risk Assessment**
- **3 Most Common Causes of Perioperative Reactions**
 - **Neuromuscular Blocking Drugs**
 - **Latex**
 - **Antibiotics**

Scope of the Problem

- True incidence of anaphylaxis, and the associated morbidity and mortality, remains poorly defined
 - Depending on the country, hypersensitivity reactions represent 9-19% of complications associated with anesthesia
 - 1 in 3,500 – 1 in 13,000
 - Mortality rate: 5-7%

The Past Predicts the Future

- **Identification of Risk Factors for Perioperative Anaphylaxis**
 - Detailed history – determine if it was truly anaphylaxis
 - Review of medical and past anesthesia records

Anesthesia-Related Anaphylaxis

- **Differs from non-anesthesia associated anaphylaxis**
 - Early signs and symptoms (malaise, pruritus, dizziness, dyspnea) are absent in the anesthetized patient
 - Cutaneous signs difficult to observe (draping)
 - Nonspecific nature of many other signs (tachycardia, hypotension, increased airway resistance)
- **Most common initial features:**
 - Pulselessness
 - Difficulty to ventilate
 - Desaturation

Anesthesia-Related Anaphylaxis

- Allergic reactions are usually more severe than non-immune mediated reactions
- Absence of cutaneous symptoms does not exclude the diagnosis of anaphylaxis
- Clinical features can occur in isolation (sudden cardiac arrest)
- Onset can occur at any time during anesthesia
 - 90% occur with induction of anesthesia
 - Seconds to minutes after infusion of agents
 - Early: NMBDs, antibiotics
 - Delayed: latex, volume expanders, dyes
- Progression slow to rapid

Anesthesia-Related Anaphylaxis

Differential Diagnosis of Anaphylaxis During Anesthesia
Drug overdose and interactions
Cardiac/vascular drug effects
Asthma
Arrhythmia
Myocardial infarction
Pericardial tamponade
Pulmonary edema
Pulmonary embolus
Tension pneumothorax
Hemorrhagic shock
Venous embolism
Sepsis
C1 esterase inhibitor deficiency
Mastocytosis
Malignant hyperthermia (succinylcholine)
Myotonias and masseter spasm (succinylcholine)
Hyperkalemia (succinylcholine)

Anesthesia-Related Anaphylaxis

At Risk Group	Drug or Drug Class
Definite Risk	
Drug Allergy	Another Drug
Multiple Surgeries, Spina Bifida, Neural Tube Defects, Bladder Catheterization, Health Care Workers	Latex
Food Allergy	
Avocado, banana, chestnut, kiwi, papaya	Latex
Soy or egg	Propofol
Gelatin	Plasma expanders
Penicillin Anaphylaxis	Penicillin, Cephaloparin
Effect Insufficient for Intervention	
Allergy/Atopy	Latex, Antibiotics
Fish Allergy	? Protamine
Asthma	All drugs
Female sex	NMBDs
Allergy to NMBDs	Propofol
No or insignificant effect demonstrated	
Previous exposure	NMBDs
Family history of anesthetic anaphylaxis	All drugs
Previous minor reaction	All drugs

Neuromuscular Blocking Agents

- Most commonly incriminated agents – 50-70%
- Not all NMBAs equally likely to cause reactions
 - Most likely: suxamethonium
 - Least likely: pancuronium, cisatracurium
 - Possibly higher risk: rocuronium
- Cross-sensitization is common – 60-70%
 - However, allergy to all NMBAs unusual
- Prior exposure is not necessary – 15-50% of reactions occur with first exposure
 - ? Cross-reaction with other chemicals

Neuromuscular Blocking Agents

- **Non-Immunologic (non-IgE mediated) reactions also can occur (20-50% of NMBA reactions) to:**
 - **D-tubocurarine**
 - **Atracurium**
 - **Mivacurium**
- **Direct mast cell release**
- **Generally less severe than IgE-mediated reactions**

Neuromuscular Blocking Agents

- Evaluation
 - Routine testing not recommended – low PPV
 - If history of anaphylaxis to NMBA, the skin test (PST and ID) – high PPV
 - PST – start with undiluted drug except for succinylcholine, atracurium, mivacurium (5X and 10X dilutions)
 - ID – 0.03-0.05ml of 1/1000 – 1/100 dilutions
 - No currently available commercial in vitro assay

Latex

- **Second most commonly incriminated cause**
 - Up to 17% in general population
 - 27-76% in pediatric population
- **Risk factors**
 - Children with multiple surgeries, spina bifida, neural tube defects, urogenital malformations
 - Adults with multiple surgeries
 - Health care workers
 - Plant food allergy (avocado, banana, chestnut, kiwi)
 - Atopics

Latex

- **Diagnosis**

- Questionnaire not sufficiently reliable to diagnose latex allergy
- Sensitization \neq Allergy
 - 12.5% of anesthesiologist have latex-specific IgE
 - 2.4% of anesthesiologist have symptoms with latex exposure
- Skin testing – not standardized
- In vitro latex-specific IgE determination – sensitivity of 73-93%

- **Management**

- AVOIDANCE

Antibiotics

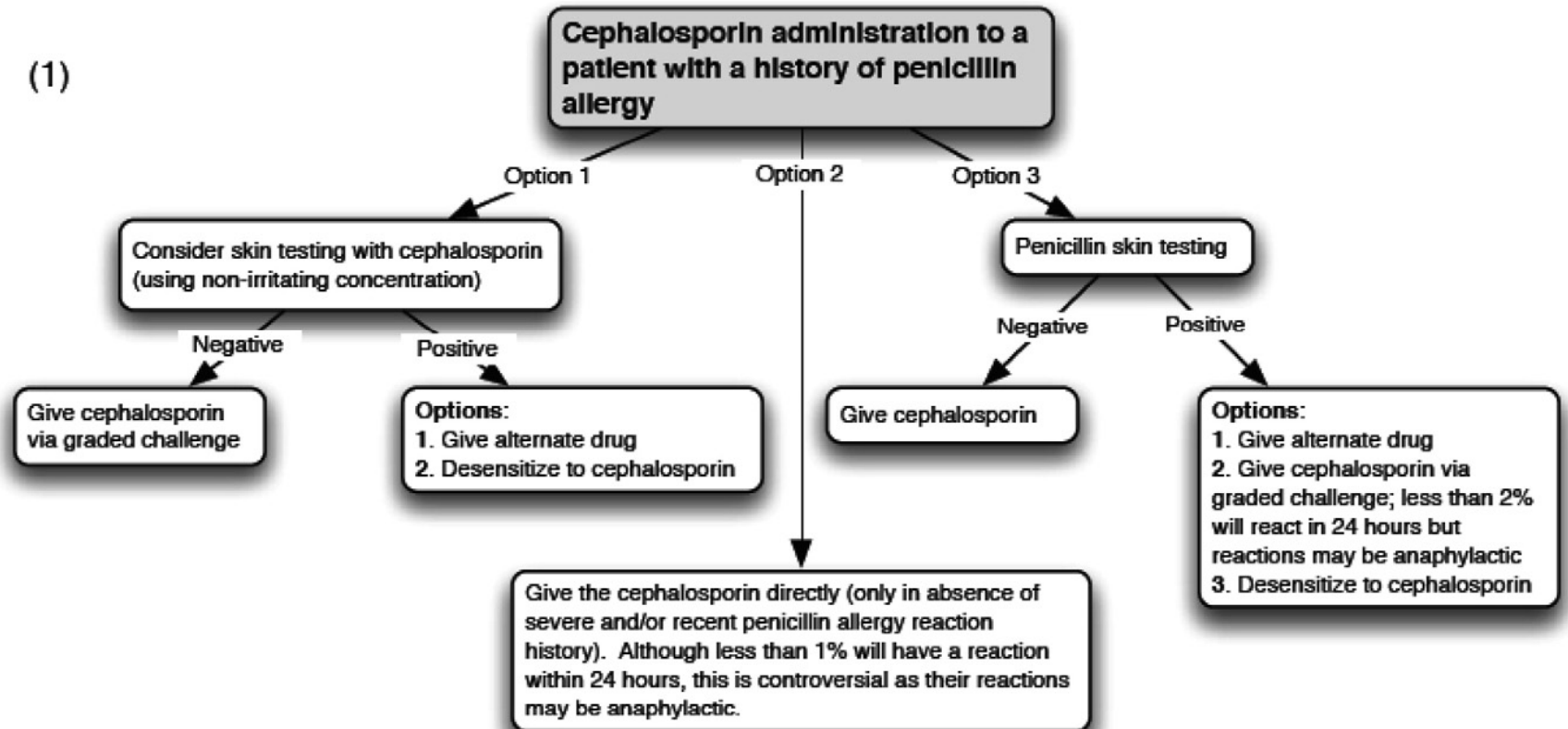
- Penicillins and cephalosporins responsible for 70% of perioperative reactions to antibiotics
- History of penicillin allergy is not very reliable
 - Only 10-20% of patients who report PCN allergy have a documented allergy
- Cephalosporin allergy – overall rate 10-fold lower than penicillin allergy
 - 2% of PCN skin test + patients react to cephalosporins
- Vancomycin reactions – 5-14% of adults get red man syndrome (flushing, pruritus, erythematous rash, hypotension) – usually related to rapid infusion rate

Antibiotics

- **Diagnosis**
 - **Skin testing to major and minor PCN determinants**
 - **NPV 97%**
 - **PPV 40-60%**
 - **Skin testing to cephalosporins not standardized**
 - **Positive ST using non-irritant concentration suggests presence of drug specific IgE**
 - **Negative ST does NOT rule out allergy as NPV is unknown**

Antibiotics

(1)

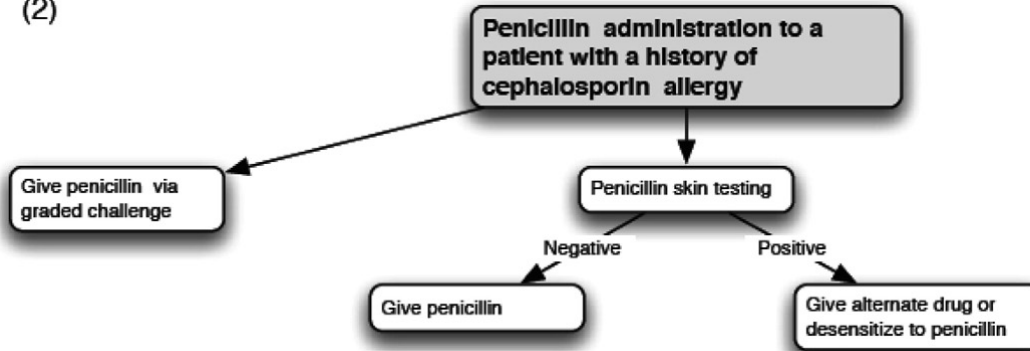


Drug Allergy: An Updated Practice Parameter

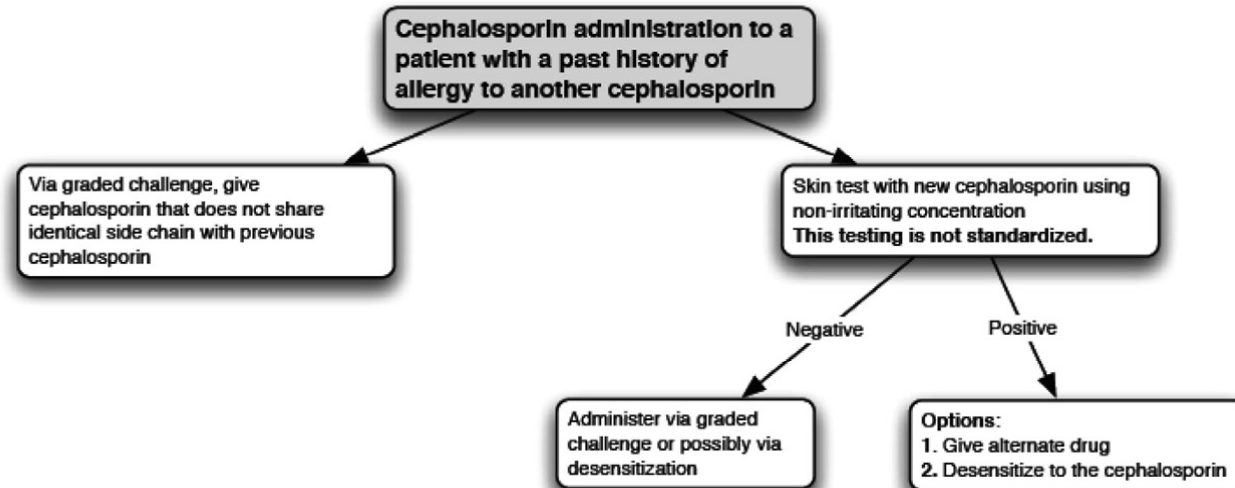
These parameters were developed by the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology.

Antibiotics

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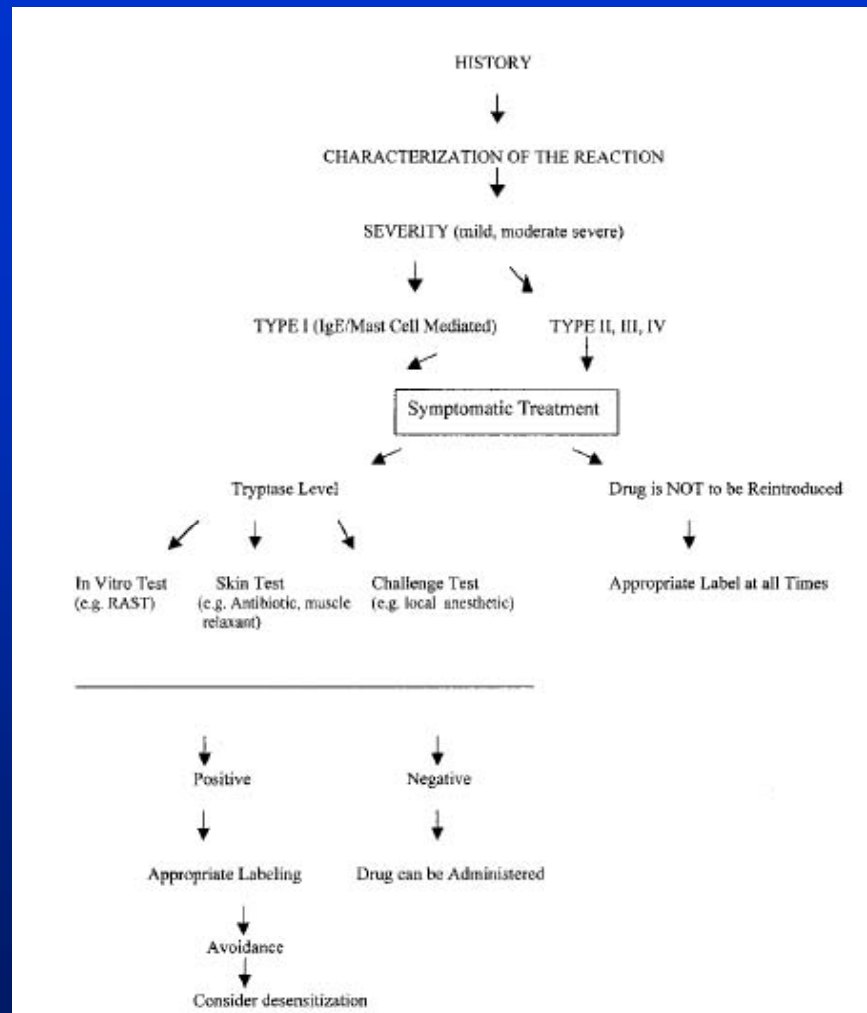


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Anaphylaxis during the perioperative period.

Hepner DL, Castells MC. Anesth Analg. 2003



Anaphylaxis during the perioperative period.

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Table 1. Drugs Involved in Perioperative Anaphylaxis (5)

Substance	Incidence of perioperative anaphylaxis (%)	Most commonly associated with perioperative anaphylaxis
Muscle relaxants	69.2	Succinylcholine, rocuronium, atracurium
Natural rubber latex	12.1	Latex gloves, tourniquets, Foley catheters
Antibiotics	8	Penicillin and other β -lactams
Hypnotics	3.7	Propofol, thiopental
Colloids	2.7	Dextran, gelatin
Opioids	1.4	Morphine, meperidine
Other substances	2.9	Propacetamol, aprotinin, chymopapain, protamine, bupivacaine

Populations at risk

Common variable immunodeficiency

Mastocytosis

Mast cell activation syndrome

Clinical Vignette

- 48 y o female healthy until 6 months ago admitted to BWH with cough, dyspnea, sputum, fever and chest pain
- XR : LLL infiltrate
- CT: bronchiectasis
- PMH: recurrent sinusitis X 3 years, SVT
gum infections, pernicious anemia
SOH : 2 children, nurse, non smoker

Clinical Vignette

- IgG 58 mg/dl (NI: 700 mg/dl)
- IgA undetectable (NI: 70 mg/dl)
- IgM 10 mg/dl (NI: 40 mg/dl)
- CBC/Diff : nl

CVID

- CVID is the most common immunodeficiency after IgA deficiency.
- It has an estimated prevalence of 1:10000 to 1:200,000 and it affects both male and females.
- Incidence is approximately 1:50,000
- Most cases are sporadic, but at least 10-20% are familial, with a predominance of autosomal dominant over autosomal recessive inheritance. In familial cases, both CVID and selective IgA deficiency (IgA < 7mg/dl) can be seen.

CVID -Laboratory features

- Patients with CVID have a deficiency of IgG that is usually associated with low levels of one or more other isotypes (IgA or IgM).
- Mean IgG level=246 mg/dl
- IgA is less than 10mg/dl in 70% of patients
- IgM is less than 25mg/dl in 80% of patients.
- There is an inverse relationship between the age of the subject and serum IgM: younger patients are more likely to have lower IgM levels at the time of diagnosis.

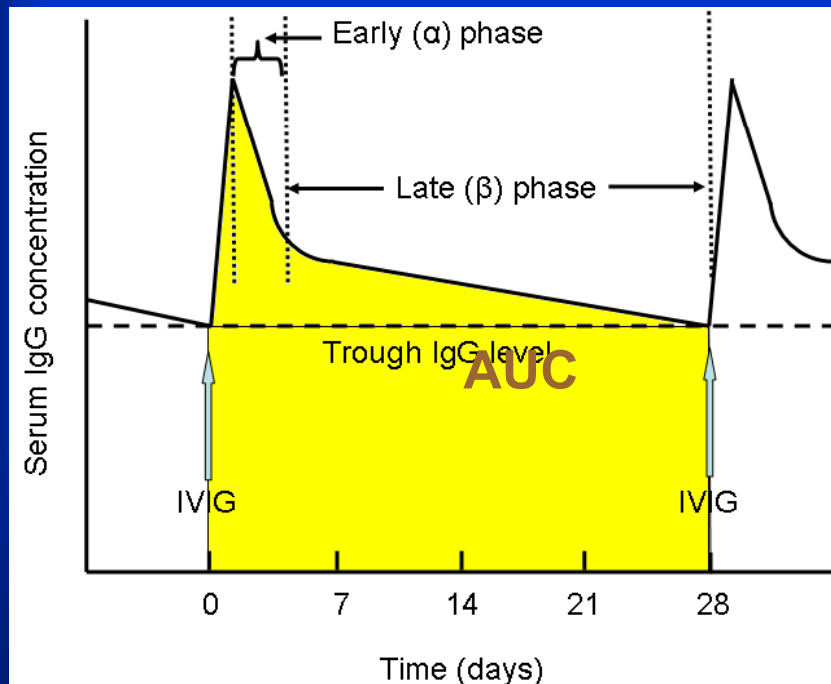
CVID Complications/associated conditions

- Severe infections in the perioperative period:
 - adequate replacement IgG
 - antibiotic coverage
- Anaphylactic reaction from IgG preparations with high IgA content:
 - low IgA products
 - sq IgG preparations

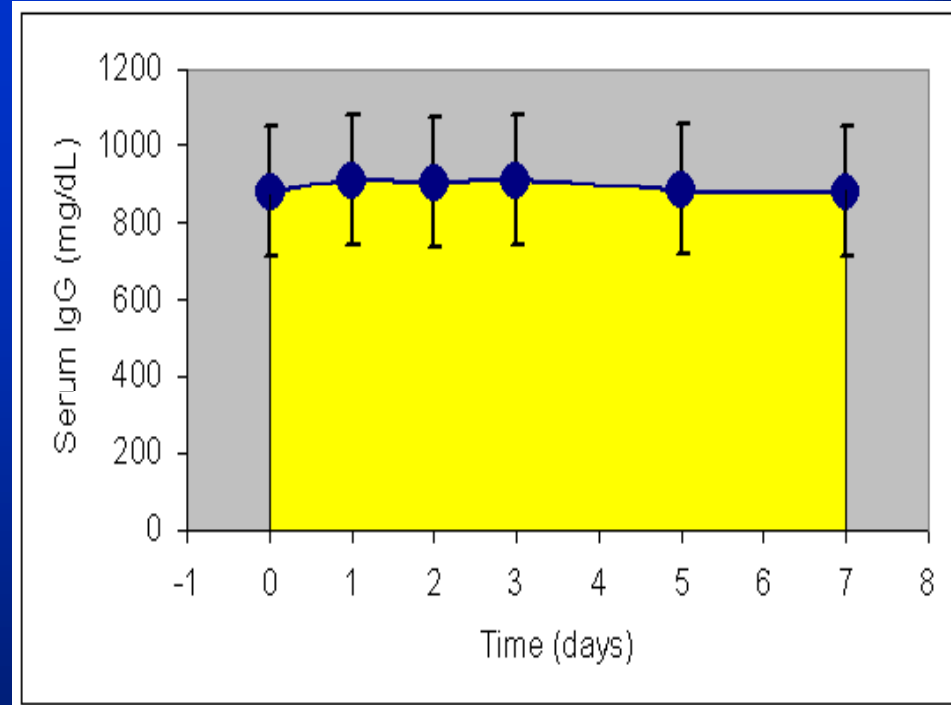
Indications for therapy

- IgG : IVIG and SQ IgG
 - 1st line for agammaglobulinemia, CVID, class-switch defects, some secondary hypogam.
 - 2nd line for any dysgammaglobulinemia or antibody production defect for which antibiotic prophylaxis is ineffective or is not tolerated
- Antibiotic prophylaxis
 - IgG subclass def., specific antibody def., IgA def (w or w/o IGGSD), transient hypogam.

IgG pharmacokinetics



From Bonilla, FA, Immunol Allergy Clin N Am 2008; 28:803.



From Berger M. Subcutaneous IgG therapy in immune deficiency diseases. In: Clinical focus on primary immune deficiencies, issue 13. Towson (MD): Immune Deficiency Foundation; 2008. p. 2.

Mastocytosis: Definition

- An abnormal increase in tissue mast cells affecting:
 - Skin
 - Bone marrow and bones
 - Gastrointestinal tract
 - Liver
 - Spleen
 - Lymph Nodes

Mastocytosis

- Cutaneous

Accumulation of mast cells in skin

Urticaria Pigmentosa, Mastocytoma, Diffuse (DCM), Macular Telangiectasia (TMEP)

- Systemic :

Accumulation of mast cells in bone marrow and in other organs

Criteria : 1 Major + 1 Minor or 3 Minor

Systemic Mastocytosis

Diagnostic Criteria

Major Criteria :

Leukemia Research 2001

multifocal infiltrates of 15 or more mast cells in bone marrow and/or extracutaneous organs

Minor Criteria:

- > 25% spindle shaped mast cells
- c-kit mutations (codon 816)
- aberrant expression of CD2 and CD25
- Tryptase >20 ng/ml

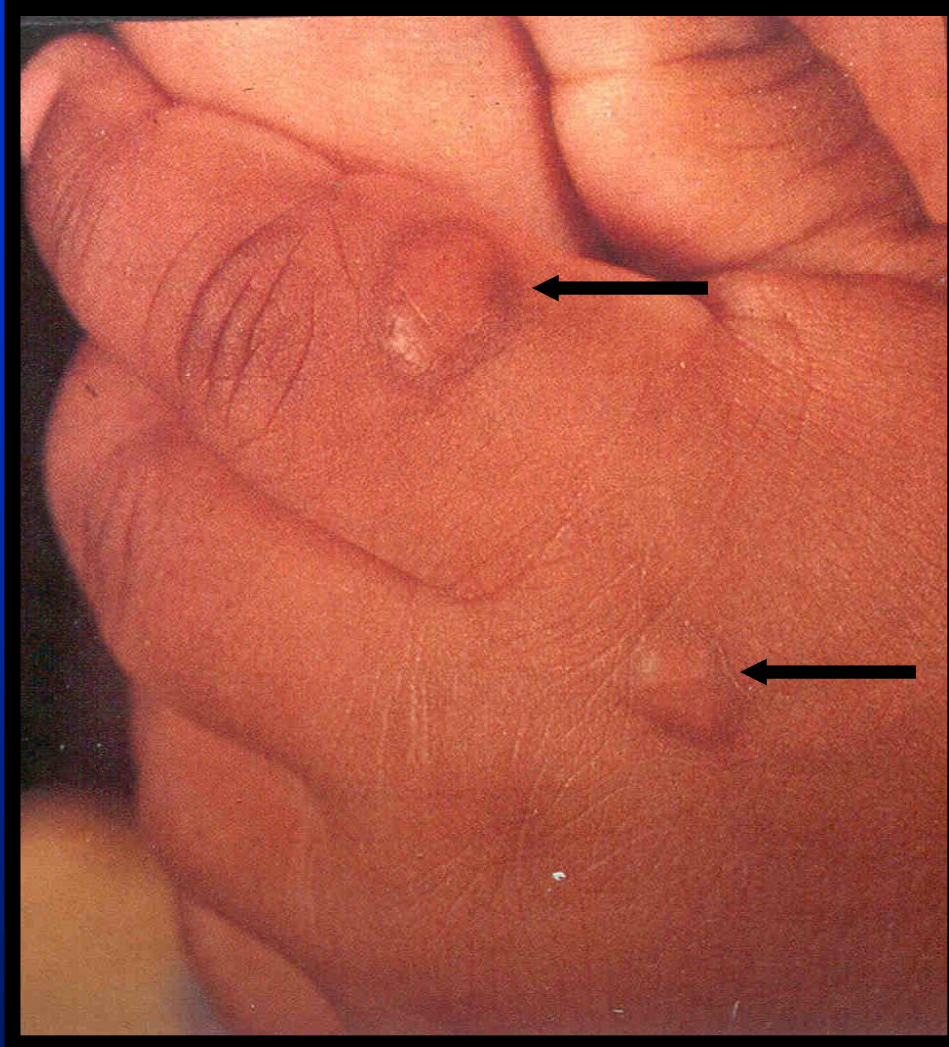
Cutaneous Mastocytosis

- Limited to the skin
- Forms:
 - Urticaria Pigmentosa
 - Solitary mastocytoma
 - Diffuse cutaneous mastocytosis
 - Telangiectasia macularis eruptive perstans
- Pathology: increased numbers of subepidermal and epidermal accumulations of mature, scroll-poor tryptase and chymase positive mast cells, frequently in perivascular locations

Urticaria Pigmentosa



Mastocytoma



Triggers for Mast Cell Mediator Release

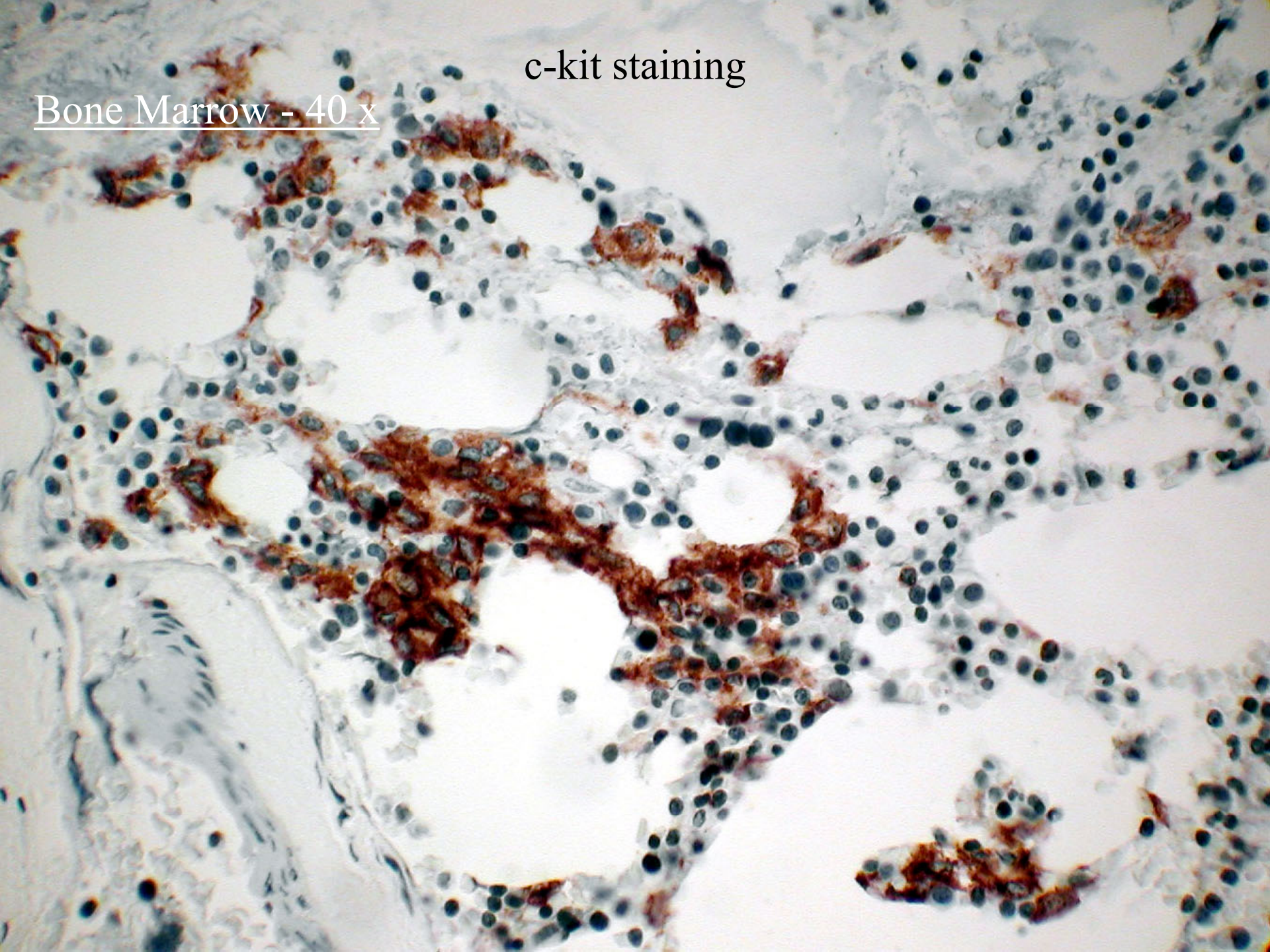
- Insect Stings, Poisons:
 - Hymenoptera/Ants
 - Jellyfish
 - Snakes
- Drugs:
 - Codeine
 - Morphine
 - Narcotic Analgesics
 - Aspirin and Non-steroidal anti-inflammatory drugs
 - Muscle Relaxants
 - Others
- Changes in Temperature:
 - Heat
 - Cold
- Alcohol
- Mechanical Irritation:
 - Massage
 - Friction
- Infections:
 - Bacterial
 - Viral
 - Ascaris
- Bacterial Toxins:
 - Fish
- Others:
 - Anesthesia
 - Surgery
 - Invasive Procedures
 - Endoscopic procedures

Case # 2

- Anaphylaxis 1 q month for 9 years
Flushing, explosive N/V/D, hypotension, syncope, DH
ER :fluids,steroids, epi,
- Triggers: alcohol, stress, emotions, infections, foods, NSAIDS
- Complaints: flushing, chronic fatigue, depression, anxiety, bone pain and FX, chest pain (multiple MI r/o)
- PE: few macular lesions in chest compatible UP

Bone Marrow - 40 x

c-kit staining



Case #3

30 y o male severe osteoporosis of both hips

Bilateral hip prosthesis

Gastrointestinal symptoms

Inability to concentrate, mental fogginess

Tryptase : 60 ng/ml

Review of the slides from the hip surgery revealed
aggregates of >50 mast cells, spindle shaped

Populations at risk

Common variable immunodeficiency

Mastocytosis

Mast cell activation syndrome

Case #1

- 44-year-old female referred to Allergy & Immunology for Idiopathic Anaphylaxis, no UP
- 4 years prior developed seasonal rhinitis and was skin test + grasses, weeds, cat
- Immunotherapy initiated (IT)
- Multiple adverse effects IT : burning hands and feet, chest pressure – received epinephrine
- 2nd episode of local reaction with lightheadedness requiring epinephrine
- IT discontinued

Case #1

- 3 years prior to presentation— developed persistent nasal congestion
- One episode — Japanese restaurant - upset stomach, tongue and facial swelling, burning hands and feet. No hives. SOB and wheezing
- ER and given epinephrine.
- 3 more similar episodes— no identifiable triggers
- Not all food related

Case #1

- In 2008: multiple episodes of severe cramping abdominal pain, nausea, vomiting, feeling very dizzy, feet and hand burning and a feeling of impending doom but no hives
- April 2008: several hours after cooking ham.
- ER: severe hypotensive to 60/30s - given epi. Resolution of symptoms and discharged home.

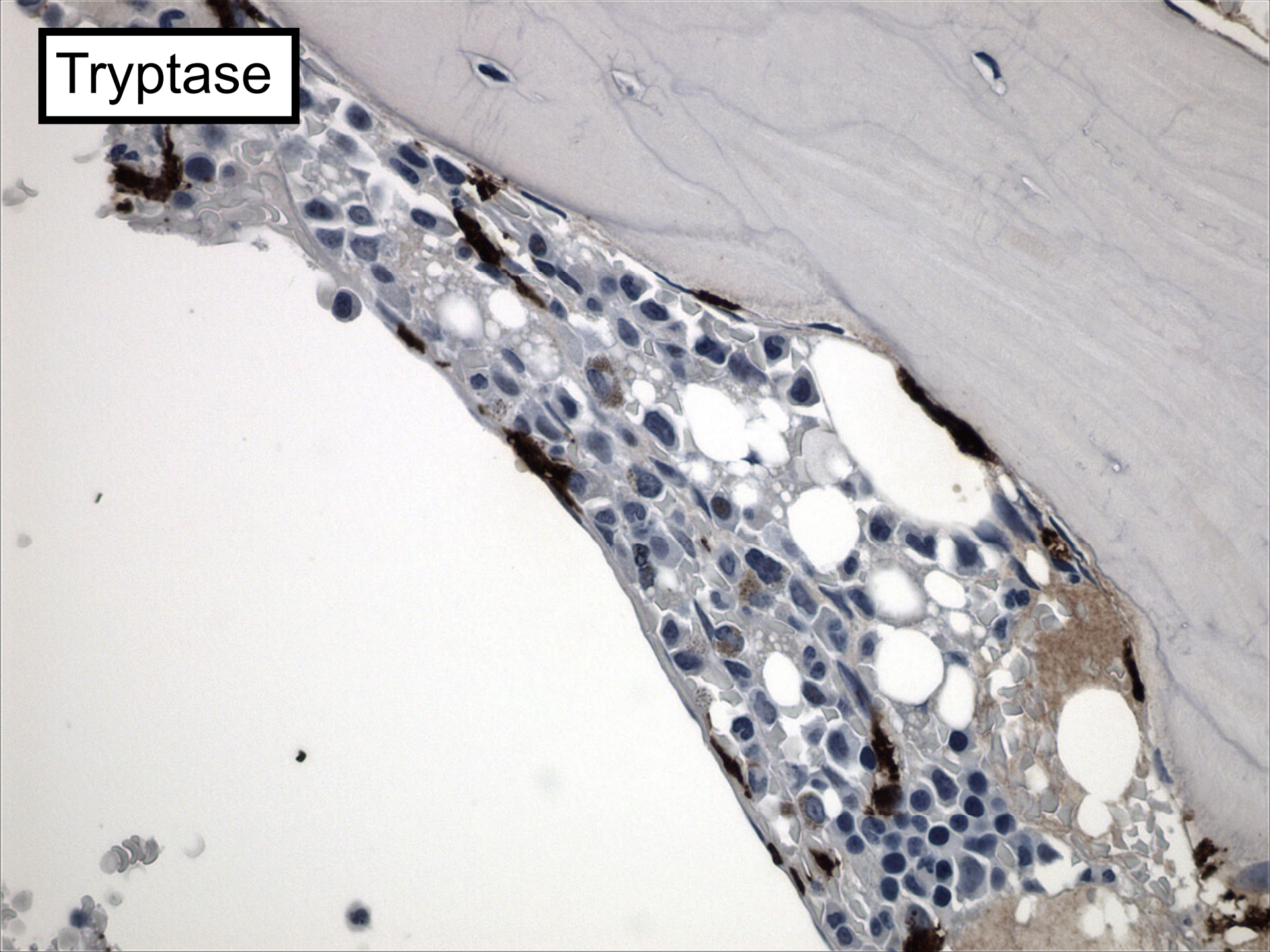
Case #1

- In 2009- monthly symptoms: starting around her menstrual cycle- burning hands and feet, nausea, vomiting, feeling of doom. No hives.
- Multiple trips to ED (> 20)
- Multiple epinephrine administration (> 30)

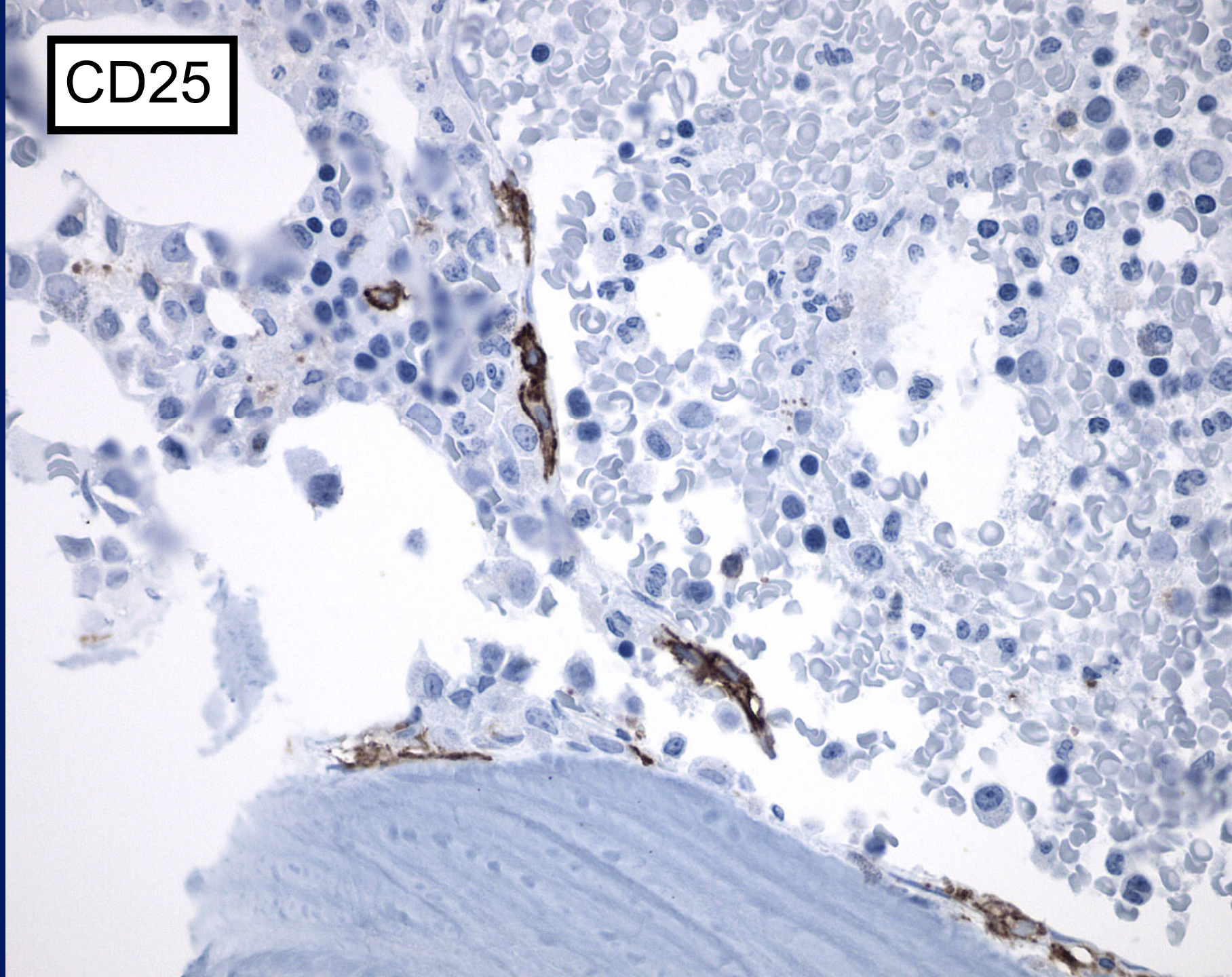
LABS

- tryptase 8.75 ng/ml total, <1 ng/ml mature
- Prostaglandin E2 308 pg WNL
- 24h urine histamine 57.6 (range 0-30)
- IgE : 18 IU/ml; Specific IgE foods (-)
- BMB: no MC aggregates, few spindle MC
- Positive CD25 MC in BM
- PB : c-kit D816V mutation +

Tryptase



CD25



Mastocytosis and Mast cell Activation Syndromes

Perioperative Risks

- Massive mast cell activation during anesthesia, surgery and organ manipulation (death reported in 1 patient during laparotomy)
- Pre-medication : anti-histamine H1 and H2
- Tryptase levels